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TITLE: Procedures and Data of Current Antidotal Therapies for Toxicants Employed as Chemical Warfare Agents

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demonstrated a relatively rapid and effective mechanism by which such procedures				
	and data can be peer reviewed by qualified and experienced scientists and then			
presented to other interested researchers. The time from receipt of the first manuscript to special issue publication was nine months. Conclusions are presented				
which will provide a model for other future special issues to follow and identify				
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FOREWORD

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Introduction

The findings from U.S. Army-sponsored medical chemical defense research projects are of interest and benefit to other scientists engaged in similar or related work either with chemical agents or industrial chemicals, e.g., pesticides, raw materials, byproducts, pollutants, etc. Toxicology is a scientific discipline predominately interested in the results of such research. At present, there are no peer-reviewed scientific journals that strictly focus on presenting comprehensively, the procedures, data and results from medical chemical defense research. Researchers desiring to make such data available to the general scientific community must submit manuscripts to peer-reviewed journals that often do not have an editorial board experienced enough with such work to provide a proper scientific review. As a result, this work becomes fragmented and diluted in both time and content in the peer reviewed literature. This is at least one reason why it is difficult for interested scientists to stay informed with this area of research by reading only the current, peer reviewed, literature.

The Journal of the American College of Toxicology is a peer-reviewed journal routinely produces special peer-reviewed issues sponsored by industry and government organizations on topics of interest to a readership that is international in scope. Several members of the American College of Toxicology have significant first hand experience in conducting government-sponsored scientific research into medical chemical defense related problems. Therefore, production of a special issue of the Journal of the American College of Toxicology (JACT) was proposed for sponsorship by the U.S. Army Medical Research and Development Command to present, in one place, original articles presenting up-to-date findings on a variety of issues at the cutting edge of medical chemical defense research.

Topics identified as being of general interest to the readership included: findings from studies involving unique antidotal therapies, studies to investigate the mechanism(s) of action of chemical agents or their antidotes, presentation of methods used to develop or screen antidotes, and the presentation of new experimental designs that reduce animal usage requirements or that incorporate *in vitro* procedures in useful and cost effective ways in the evaluation of medical chemical defense problems.

The principal objective of this project was to:

"Develop and disseminate a peer-reviewed scientific document whereby procedures and data of current antidotal therapies for toxicants employed as chemical warfare agents might be shared openly with other interested scientists."

In order to accomplish this objective the following milestones were identified.

- Assemble a group of qualified editors and scientific reviewers capable of properly assessing the merit of each manuscript submitted to the Journal of the American Toxicology readership.
- Solicit and obtain manuscripts from researchers involved with cutting edge work in the medical chemical defense area.
- Review each manuscript submitted first for appropriateness of content and then for technical merit and make a decision with respect to the inclusion of each manuscript in the special journal edition.

- Obtain any necessary revisions to accepted manuscripts and produce the special issue as quickly as possible.
- Publish the peer-reviewed manuscripts in a special edition of the JACT Journal and distribute the edition to the readership.

Our goal was to produce the special issue in one year's time or less after receipt of the first manuscript.

Description of the Work

The project was initiated with partial funding beginning in September 1995. The remaining funds necessary to complete the project as proposed were provided in September 1996. The current Editor-in-Chief of the JACT, Dr. Robert Diener, being a veterinarian and widely experienced toxicologist as well as having excellent editorial and journal production credentials was designated as the Lead Editor for the special edition. The responsibility of the Lead Editor was to provide the initial format and content review on all articles submitted and to determine their suitability for further peer review and inclusion in the special issue. The Lead editor also served as a third peer reviewer for manuscripts that required a tie breaking accept or reject decision based on the results of the peer review. In order to assist Dr. Deiner in this process, it was necessary for the American College of Toxicology to select, from its membership, a qualified scientist with current experience in the field of medical chemical defense research.

Dr. David Hobson, a toxicologist/pharmacologist and long standing American College of Toxicology member who is well experienced with research involving a diversity of current medical chemical defense research issues was identified as the Co-Editor for the special edition and as the U.S. Army point-of-contact within the American College of Toxicology responsible for this project. The Co-Editor served as an expert consultant to Dr. Diener and coordinated the peer review process. The Co-Editor was also designated to prepare the final project report.

Ms. Carol Lemire, Executive Secretary of the American College of Toxicology served as the Administrative Coordinator for the project with Ms. Eve Kagan as her administrative assistant. The responsibility of the Executive Secretary was to serve as the principal point of contact with the U.S. Army Medical Research and Development Command for coordination of project financing and correspondence.

Qualified and interested reviewers for the manuscripts deemed suitable for inclusion in the special edition were solicited primarily from the ACT membership and included individuals with both *in vivo* and *in vitro* experience in conducting medical chemical defense research.

Appendix A provides a listing of all individuals and their roles in the completion of this project.

Next, the co-Editors provided guidance for submission of manuscripts for the special edition to the U.S. Army Medical Research and Development Command for dissemination to interested scientists currently working on government-funded medical chemical defense research projects. The principal point of contact for this activity was COL David Moore, U.S. Army Medical Research Institute for Chemical Defense.

The first manuscripts submitted for inclusion in this issue were received at the offices of Dr. Diener in April 1996. A total of 25 manuscripts were submitted over an approximate three month period.

The preliminary review for suitability of content was accomplished by Drs. Diener and Hobson and resulted in:

- Rejection of three manuscripts due to subject matter and content more suitable for other readerships (e.g., Analytical Chemistry) not well represented by that of the JACT readership,
- Identification of 15 manuscripts suitable for inclusion in the special edition and to receive full peer review.
- Seven manuscripts being identified as having subject matter general enough so as to be more suitable for inclusion in a regular edition of the JACT rather than the special edition on medical chemical defense.

Following the peer review, one additional manuscript was rejected, 11 manuscripts were returned with corrections in time to be included in the special edition, and three manuscripts were included in the list of those to be published in a regular edition of the JACT when they were returned with corrections.

Appendix B provides a disposition summary for the manuscripts received for review. Due to the sensitive and confidential nature of the scientific peer review process, the outcome of each individual peer review is not provided, but the overall disposition of the manuscripts is provided. Although the manuscripts differed in quality, the overall assessment was that of good to excellent quality for all manuscripts received relative to well established and published standards for the JACT.

All peer reviewers used a standardized manuscript review form upon which to base their decision to accept or reject a manuscript and upon which to provide anonymous comments and suggestions to the manuscript authors to improve content of quality of the document. Appendix C shows the Manuscript Review Form used by all peer reviewers.

The initial and peer review process began in April 1996 and required about five months to complete. Essentially all manuscripts selected for inclusion in the special issue required some form of revision, in most cases minor, following the initial and peer review. The turnaround time for obtaining completed revisions for these manuscripts was about two months.

Draft compilation of the special issue began in September 1996 and was completed in November 1996.

The publisher (Lippincott-Raven Publishers, Philadelphia, PA) received the completed draft version of the special issue in November 1996 and corresponded with the Lead Editor and Co-Editor on formatting issues in November through December 1996.

The special issue of the JACT was designated as Volume 15, Supplement 2, 1996, "Special Issue on Chemical Defense Toxicology." Pre-distribution copies of the issue were forwarded to the U.S. Army Medical Research and Development Command, via COL David Moore in January 1997. Copies of the special issue were mailed to and received by the ACT membership in February 1997.

Conclusions

The special issue met its objectives by providing a collection of peer reviewed, manuscripts covering a broad range of topics of interest and scientific value to the readership. The total time from the first manuscript submission and final publication was nine months. Relative to the time required to obtain peer review and publication of this number of manuscripts in a diversity of other scientific journals, review and publication occurred relatively rapidly and were not subject to the hazards of scrutiny and judgment of scientific merit by reviewers with little or no experience in this aspect of biomedical research.

The production of the special issue also demonstrated a potential and mechanism for future collaborations between U.S. Army sponsored research groups investigating medical chemical defense problems and the proper peer review and timely publication of their findings in an internationally recognized scientific journal. Such future collaborations could occur as special issues planned in advance to coincide with the completion or reporting of findings from several research groups such as annual bioscience reviews, interim reporting, etc.

Future collaborations would most likely be able to occur at reduced cost and time requirements to the government due to the identification of ways to increase manuscript submission and review process efficiency learned during completion of this project. Examples of these include the following:

- The manuscript submission date should be coordinated to coincide closely with a U.S. Army Medical Research and Development Command reporting requirement or invitation to present results at a U.S. Army organized meeting or research review.
- The special edition editors and peer reviewers should be selected prior to manuscript submission.
- All mechanisms (communication systems, manuscript review forms, formatted responses from the editors to the peer reviewers and authors, cost accounting practices, etc.) should be established and in place completely prior to receipt of the first manuscript.
- The editors should use a formal project plan to keep the special issue production well coordinated time wise and to be better able to identify cost and time reductions as they occur in real time rather than after the fact.

Overall, this project produced the expected document and demonstrated an effective and timely means of reporting comprehensively U.S. Army sponsored medical chemical defense research findings in a peer reviewed international journal.

Appendix A

List of Editors, Reviewers and Clerical Personnel

Personnel Principally Involved in Development, Review and Production of the Special Issue of the Journal of the American College of Toxicology, "Special Issue on Chemical Defense Toxicology."

Person	Role	Affiliation
Robert Diener, D.V.M.	Lead Editor, Final Reviewer	Consultant in Toxicology & Pharmacology, Whitehouse Station, NJ
David Hobson, Ph.D., D.A.B.T.	Co-Editor, Peer Reviewer	Director, Pharmaceutical Sciences, DPT Laboratories, San Antonio, TX
Carol Lemire	Project Liason for the American College of Toxicology	Executive Director, American College of Toxicology, Bethesda, MD
Eve Kagan	Administrative Assistant	Executive Assistant, American College of Toxicology, Bethesda, MD
Carl Olson, D.V.M., Ph.D., D.A.B.T, D.A.B.V.T.	Peer Reviewer	Research Leader, Battelle Memorial Institute, Columbus, OH
Donald Korte, Ph.D., D.A.B.T.	Peer Reviewer	Professor of Biology, Concordia University, Mequon, WI
James Blank, Ph.D., D.A.B.T.	Peer Reviewer	Principal Research Scientist, Battelle Memorial Institute, Columbus, OH
Nancy Monteiro- Riviere, Ph.D.	Peer Reviewer	Professor, North Carolina State University, Raleigh, NC
COL David Moore	Scientific Point of Contact, U.S. Army	Deputy Commander, U.S. Army Medical Research Institute for Chemical Defense
Robert Pancotti	Supervising Production Editor	Lippincott-Raven Publishers, New York, NY

Appendix B

Distribution of Manuscripts Submitted for Review

Manuscript Distribution Summary

Manuscripts Submitted	Manuscripts Rejected	Manuscripts Selected for Publication in Special JACT Issue	Manuscripts Selected for Publication in a Future Regular JACT Issue
25	4	11	10

Appendix C Manuscript Review Form

JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY (JACT) MANUSCRIPT REVIEW FORM

MANUSC	RIPT NOMBER:		
AUTHOR	:		
TITLE:			
GENERA	L ASSESSMENT (Please check appropriate box)	٠	
1.	Is JACT the proper place for publication?		
	Yes No		
2.	Is manuscript:		
	Acceptable is its present form. Acceptable, with minor revisions noted under Com Acceptable, if extensive revisions noted under Com Unacceptable. Please include reasons under Com	Comments are	naci
3.	If manuscript is acceptable, with or without revisions overall quality.	s, estimate i	1s
	A. Excellent. Innovative - Publish as soon as po		ī.a.
	C. Fair - Marginal quality, publish only if space	e is avaitab.	re.
SPECIFI	C ASSESSMENT (Answer questions appropriate to article)	YES NO	
		122 11	,
1.	Is the title clear and precise?		
2.	Is the Abstract descriptive of contents?		
3.	Are enough details presented in the Materials and Methods Sections?		
4.	Are adequate statistical evaluations of data provided?	_	
5.	Are the Figures and Tables of suitable clarity and quality?		
6.	Are authors' conclusions justified by the data?		二
7.	Is the Discussion section pertinent to the main	-	
	theme of the paper?		
8.	Are adequate and correct references provided?		
9.	Could the paper be improved by shortening?		_
10.	Are organization, style and grammar satisfactory?		
II.	Could the paper be presented as a Short Communication rather than as a regular article?		
12	Are appropriate ethical standard for the experimental		
	use of live animals followed?		

Please detach and sign original only

Signature

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COMMENTS WHICH	MAY BE TRANSMITTED TO AUTHOR	
GENERAL		
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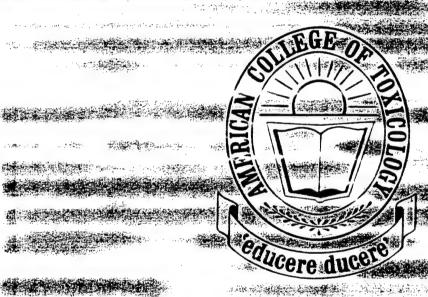
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Appendix D

Cover, Table of Contents, Title Page and Introduction from the Special Issue on "Chemical Defense Toxicology"

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Journal of the American College of Toxicology

Volume 15, Supplement 2 1996

SPECIAL ISSUE ON CHEMICAL DEFENSE TOXICOLOGY

David W. Hobson Robert M. Diener Co-Editors

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Journal of the American College of Toxicology

Special Issue on Chemical Defense Toxicology

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Volume 15, Supplement 2 1996

Lippincott-Raven Publishers

Introduction

The development and use of chemical agents as strategic weapons in the modern sense began in the early part of this century. Since then, toxicologists and scientists in many disciplines have engaged in research to understand the mechanisms by which chemicals such as sulfur mustard, phosgene, cyanides, and acetylcholinesterase inhibitors act and to develop effective treatments that will eliminate or reduce the threat that such agents pose to military personnel.

As we approach the end of this century, it is sobering to think that, in some parts of the world, the threat posed by the use of chemical agents as weapons to achieve a military objective or to invoke terror in civilian populations remains real. Furthermore, despite important progress made toward understanding the mechanisms of toxic injury for some of these agents, and despite the many significant developments achieved in finding and implementing effective treatments and prophylactic measures against these agents, much work remains to be done.

The purpose of this supplement to *Journal of the American College of Toxicology* is to share some of the more recent findings in the important area of chemical defense toxicology. We hope to stimulate scientific thought and dialogue toward understanding the toxicology of the existing chemical agents so that safe and effective countermeasures can be developed and the threats that these agents pose can be reduced.

The American College of Toxicology acknowledges the invaluable assistance of some of its members who are knowledgeable in this area of research and the U.S. Army Medical Research and Development Command in the production of this supplement. The Editors also thank Col. David Moore and other scientists at the U.S. Army Medical Research Institute for Chemical Defense for their technical assistance and advice during the preparation of this supplement.

We hope that you will find this supplement both informative and scientifically interesting.

David W. Hobson, Ph.D., D.A.B.T. Co-Editor

Personnel Receiving Pay (Direct or Indirect) from Cooperative Agreement DAMD17-95-2-5032

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